K110620

MAY - 3 2011

Meridian Bioscience, Inc.	510(k) Application Premier *C. difficile* GDH	
	Description:	510(k) Summary Premier *C. difficile* GDH
	Identification:	Attachment 002
	Date:	March 01, 2011

510(k) number: _____ **Date of Preparation:** March 01, 2011

Submitter:	**Meridian Bioscience, Inc**
Submitter's address:	3471 River Hills Drive Cincinnati, Ohio 45244
Contact:	Susan Bogar
Contact number:	(513) 271-3700
Device name:	Premier *C. difficile* GDH
Common name:	Enzyme Immunoassay for *C. difficile* Common Antigen
Classification:	Antigen, *C. difficile* MCB, CFR Section 866.2660
Predicate device:	K030992: TECHLAB C. DIFF CHEK™ – 60 ELISA
Reference comparator:	Bacterial culture

Description of the device:

Premier *C. difficile* GDH is a qualitative enzyme immunoassay screening test to detect *Clostridium difficile* antigen, glutamate dehydrogenase, in fecal specimens from symptomatic persons suspected of having *C. difficile* infection (CDI). The assay consists of Premier *C. difficile* GDH Microwells coated with polyclonal antibodies specific to *C. difficile* GDH, Premier *C. difficile* GDH Enzyme Conjugate, Premier 20X Wash Buffer II, Premier Substrate I, Premier Stop Solution I, Premier *C. difficile* GDH Sample Diluent/Negative Control, and Premier *C. difficile* GDH Positive Control.

Intended Use:

Premier *C. difficile* GDH is a qualitative enzyme immunoassay screening test to detect *Clostridium difficile* antigen, glutamate dehydrogenase, in fecal specimens from symptomatic persons suspected of having *C. difficile* infection (CDI). This test does not distinguish between toxigenic and non-toxigenic strains of *C. difficile*. Samples from symptomatic patients that produce positive results with this test must be further tested with an assay designed to detect toxigenic *C. difficile* strains and assist with the diagnosis of CDI.

Table 1: Comparison to predicate device.

Characteristic	Premier *C. difficile* GDH	TECHLAB C. DIFF CHEK-60
Test Format	ELISA Microplate	ELISA Microplate
Intended Use		
Qualitative/Quantitative	Qualitative	Qualitative
Target Antigen	*Clostridium difficile* glutamate dehydrogenase	*Clostridium difficile* glutamate dehydrogenase
Screening, Diagnostic, or Identification Test	Screening	Screening
Specimen Types		
Human Stool Unpreserved	Yes	Yes
Reagents/Components	Premier *C. difficile* GDH Microwells Premier *C. difficile* GDH Enzyme Conjugate Premier 20X Wash Buffer II Premier Substrate I Premier Stop Solution I Premier *C. difficile* GDH Sample Diluent/Negative Control Premier *C. difficile* GDH Positive Control	Microassay plate Enzyme Conjugate 20X Wash Buffer Substrate Stop Solution Diluent Positive Control
Diagnostic Marker		
Antibody	Yes	Yes
Antibody Sources		
Solid phase (microplate)	Rabbit polyclonal	Polyclonal
Enzyme Conjugate	Rabbit polyclonal	Mouse monoclonal
Sample Preparation		
Unpreserved liquid/semi-solid stool	50 µL of thoroughly mixed stool into 200 µL Sample Diluent. Vortex for 15 seconds.	50 µL specimen into 200 µL Diluent. Vortex for 10 seconds.
Testing Time	Approximately 60 minutes	Approximately 60 minutes
Equipment		
General Laboratory Equipment	Spectrophotometer StatFax™- 2200 Incubator/Shaker (optional) Semiautomated Microplate Washer (optional)	Spectrophotometer
Reading Method	Spectrophotometric	Visual Spectrophotometric
Results Interpretation		
Single Wavelength (A_{450} nm)	Negative: < 0.200 Positive: ≥ 0.200	Negative : < 0.120 Positive: ≥ 0.120
Dual Wavelength	Negative: < 0.150 Positive: ≥ 0.150 $A_{450/630}$ nm	Negative: < 0.080 Positive: ≥ 0.080 $A_{450/620}$ nm
Visual Read	N/A	Positive: Any yellow color Negative: Colorless

Performance Comparison, Non-clinical Tests

Analytical Sensitivity

Sensitivity studies were designed to determine within 95% confidence intervals the analytical limit of detection (LoD) of *C. difficile* GDH antigen diluted in a human stool matrix. The analytical sensitivity of this assay was based on 45 replicates for each measurand and with a stated probability (95%) of obtaining positive responses at the following levels of the measurand when spiked in stool: 8 ng/mL.

Interference Testing

Selected drugs and other non-microbial substances that might be present in stool samples from healthy persons or patients suspected of having *C. difficile* associated disease were added to three negative stool samples and three positive stool samples. The contrived positive specimens were prepared from a pool of donor stools that were confirmed as negative. The samples were inoculated with *C. difficile* strain 11186 at 8 ng/mL, the limit of detection for this assay. Potentially interfering substances were added at final concentrations of 5% V/V or greater. Dilution Controls for each sample were prepared by adding a phosphate-buffered saline solution in place of the potentially interfering substance. Each sample was tested in triplicate.

The following substances, at the specified saturated solvent/diluent concentrations, do not interfere with Premier *C. difficile* GDH test results in the final concentrations listed: Barium sulfate (5 mg/mL), Fecal fat (2.65 mg stearic acid and 1.3 mg palmitic acid/mL), Hemoglobin (3.2 mg/mL), Imodium AD® (Loperamide HCl) (6.67 x 10^{-3} mg/mL), Kaopectate® (Bismuth subsalicylate) (0.87 mg/mL), Metronidazole (12.5 mg/mL), Mucin (3.33 mg/mL), Mylanta® (Aluminum hydroxide w/ magnesium hydroxide) (4.2 mg/mL), Pepto-Bismol® (Bismuth subsalicylate) (0.87 mg/mL), Polyethylene glycol (79.05 mg/mL), Prilosec® (Omeprazol) (0.5 mg/mL), Simethicone (0.625 mg/mL), Tagamet® (Cimetidine) (0.5 mg/mL), Tums® (Calcium carbonate) (0.5 mg/mL), Vancomycin HCl (2.5 mg/mL), Whole blood (25%), White blood cells (5%).

Cross-reactivity Study

Potentially crossreactive microorganisms that might be present in stool samples from healthy persons or patients suspected of having *C. difficile* associated disease were added to a natural negative and contrived positive sample. The contrived positive specimens were prepared from a pool of donor stools that was confirmed negative. The contrived positive sample was prepared by spiking a confirmed negative sample with *C. difficile* strain 11186 at 8 ng/mL, the limit of detection for this assay. Potentially cross-reactive microorganisms were added at final concentrations of 1.2 x 10^{8} CFU/mL (bacteria or fungi) or final concentrations greater than 1 x 10^{5} $TCID_{50}$/mL (viruses). Dilution controls for each sample were prepared by adding a 0.85% saline solution in place of the potentially cross-reactive organisms.

The following microorganisms, at the indicated concentrations, do not interfere with Premier *C. difficile* GDH test results: *Aeromonas hydrophila, Bacillus cereus, Bacillus subtilis, Bacteroides fragilis, Campylobacter coli, Campylobacter fetus, Campylobacter jejuni, Candida albicans, Citrobacter freundii, Clostridium butyricum, Clostridium bifermentans, Clostridium histolyticum, Clostridium novyi, Clostridium perfringens, Clostridium septicum, Clostridium sordellii, Clostridium tetani, Enterobacter aerogenes, Enterobacter cloacae, Enterococcus faecalis, Escherichia coli, Escherichia coli* O157:H7, *Escherichia hermannii, Escherichia fergusonii, Helicobacter pylori, Klebsiella pneumoniae, Lactococcus lactis, Listeria monocytogenes, Peptostreptococcus anaerobius, Plesiomonas shigelloides, Porphyromonas asaccharolytica, Proteus vulgaris, Pseudomonas aeruginosa, Pseudomonas fluorescens, Salmonella* Group B, *Salmonella* Group C, *Salmonella* Group D, *Salmonella* Group E, *Serratia liquifaciens, Serratia marcescens, Shigella boydii, Shigella flexneri, Shigella sonnei, Staphylococcus aureus, Staphylococcus epidermidis,*

Vibrio parahaemolyticus, Yersinia enterocolitica, Adenovirus Type 40, Adenovirus Type 41, Coxsackievirus Strain B4, Echovirus Strain 11, Rotavirus Strain WA.

Stools spiked with *Staphylococcus aureus* (Cowan strain I) and *Clostridium sporogenes* were found to be crossreactive with Premier *C. difficile* GDH.

Strain Reactivity

C. difficile stock cultures from different sources were tested and produced positive reactions at a concentration of 5.7×10^7 cells/mL with the Premier *C. difficile* GDH assay. Strains tested were as follows: 8864, 10463, 43598, 2004052, 2004111, 2004118, 2004205, 2004206, 2005070, 2005257, 2005325, 2006240, 2007431, 2007435, 2007858, 2008016, 2008029, 2008162, 2008188, 2008341, 2008351, 2009018, 2009065, 2009066, 2009099, 2009132, 2009155, 2009277, 11186, B1, BI8, BI17, BK6, CF1, G1, J7, K12, Y1, 234, 586, 611, 620, 2C62, 2C165, C122, UNC 19904, X15076.

Performance Comparison, Clinical Tests

Clinical trials for the Premier *C. difficile* GDH assay were conducted from November 2010 to February 2011. Performance characteristics of the Premier *C. difficile* assay were determined by comparison to bacterial *C. difficile* culture. Independent clinical test sites located in the Midwestern, Southeastern and Southwestern regions of the United States evaluated a total of 733 qualified patient samples. Samples were collected from 337 (46.0%) males and 390 (53.2%) females. Gender was not defined for 6 (1%) patients. The age groups of patients range from 22 days to 99 years. No differences in test performance were observed based on patient age, gender, or geographic location. Overall sensitivity was determined to be 92.3% (95% CI: 86.0 - 95.9%). Overall specificity was determined to be 95.8% (95% CI: 93.9 – 97.1%). Subsequent tables show overall assay performance as well as performance by clinical site and patient age.

Table 2: Performance Characteristics for Premier *C. difficile* GDH

Culture	Premier *C. difficile* GDH		
	Positive	Negative	Total
Positive	108	9	117
Negative	26	590	616
Total	134	599	733
			95% CI
Sensitivity	108/117	92.3%	86.0 – 95.9%
Specificity	590/616	95.8%	93.9 – 97.1%
Correlation	698/733	95.2%	93.4 – 96.5%

Table 3: Performance characteristics by site.

Premier *C. difficile* GDH	Positive Samples				Negative Samples		
Clinical Site	Premier GDH/ Culture	Sensitivity %	95% CI		Premier GDH/ Culture	Specificity %	95% CI
Site 1	13/16	81.3%	57.0 – 93.4%		84/87	96.6%	90.3 – 98.8%
Site 2	28/30	93.3%	78.7 – 98.2%		132/140	94.3%	89.1 – 97.1%
Site 3	44/46	95.7%	85.5 – 98.8%		147/153	96.1%	91.7 – 98.2%
Site 4	15/15	100.0%	79.6 – 100%		169/175	96.6%	92.7 – 98.4%
Site 5	8/10	80.0%	49.0 – 94.3%		58/61	95.1%	86.5 – 98.3%

Table 4: Performance Data (patients less than 2 years of age)

Culture	Premier *C. difficile* GDH		
	Positive	Negative	Total
Positive	21	2	23
Negative	3	54	57
Total	24	56	80
			95% CI
Sensitivity	21/23	91.3%	73.2 – 97.6%
Specificity	54/57	94.7%	85.6 – 98.2%
Correlation	75/80	93.8%	86.2 – 97.3%

Table 5: Performance Data (patients 2 years of age and greater)

Culture	Premier *C. difficile* GDH		
	Positive	Negative	Total
Positive	87	7	94
Negative	23	536	559
Total	110	543	653
			95% CI
Sensitivity	87/94	92.6%	85.4 – 96.3%
Specificity	536/559	95.9%	93.9 – 97.2%
Correlation	623/653	95.4%	93.5 – 96.8%

Table 6: Overall results by patient age.

Premier *C. difficile* GDH	Positive Samples			Negative Samples		
Patient Age	**Premier GDH/ Culture**	**Sensitivity %**	**95% CI**	**Premier GDH/ Culture**	**Specificity %**	**95% CI**
<2 years	21/23	91.3%	73.2 – 97.6%	54/57	94.7%	85.6 – 98.2%
≥2 years to 12 years	27/28	96.4%	82.3 – 99.4%	118/122	96.7%	91.9 – 98.7%
>12 years to 21 years	10/13	76.9%	49.7 – 91.8%	72/75	96.0%	88.9 – 98.6%
>21 years	50/53	94.3%	84.6 – 98.1%	345/361	95.6%	92.9 – 97.3%
Not Defined	0/0	N/A	N/A	1/1	100.0%	20.7 – 100.0%

Reproducibility

Reproducibility panels were performed by three clinical laboratories using blind coded panels. Samples were randomly sorted within each panel to mask identities. Each panel consisted of 3 contrived moderately positive specimens, 3 contrived low positive samples, 3 contrived high- negative specimens, and 1 natural negative specimen. Panels were tested at three independent laboratories by two operators at each laboratory, twice each day over 5 non-consecutive days. The expected results were obtained with all samples by all technologists at all test sites at each time interval. Reproducibility of the assay is 100% for moderate positive, low positive, high negative, and negative samples.

As seen in the following tables, the expected results were obtained 100% of the time.

Table 7: Intra and inter assay variability data for all sites (single wavelength).

Panel Members	Sample N	Grand Mean AL	Between-Day		Between-Run		Between-Site		Total		Result
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	
PC	30	1.944	0.087	4.5%	0.124	6.4%	0.207	10.6%	0.279	14.3%	Positive
NC	30	0.053	0.006	10.6%	0.010	19.6%	0.011	21.1%	0.020	36.6%	Negative
MP 1	30	1.957	0.201	10.3%	0.256	13.1%	0.193	9.9%	0.359	18.3%	Positive
MP 2	30	1.936	0.200	10.3%	0.282	14.9%	0.285	14.7%	0.398	20.6%	Positive
MP 3	30	1.758	0.100	5.7%	0.205	11.7%	0.505	28.7%	0.522	29.7%	Positive
LP 1	30	0.705	0.066	9.4%	0.096	13.6%	0.092	13.1%	0.153	21.7%	Positive
LP 2	30	0.670	0.066	9.9%	0.090	13.4%	0.150	22.4%	0.184	27.4%	Positive
LP 3	30	0.694	0.055	8.0%	0.095	13.7%	0.120	17.3%	0.189	27.2%	Positive
HN 1	30	0.057	0.006	10.7%	0.008	14.2%	0.016	27.7%	0.017	29.7%	Negative
HN 2	30	0.058	0.008	13.8%	0.011	18.5%	0.016	27.1%	0.017	29.5%	Negative
HN 3	30	0.059	0.008	13.1%	0.012	20.3%	0.015	24.6%	0.024	39.8%	Negative
WN 1	30	0.050	0.002	3.0%	0.002	4.4%	0.014	28.4%	0.013	25.4%	Negative

Legend: PC=Positive control, NC=Negative control, MP=Moderate positive, LP=Low positive, HN=High negative, WN=Weak negative

Interpretation of Results at OD_{450}:

Positive Control: ≥ 0.600

Negative Control: < 0.150

Positive: ≥ 0.200

Negative: <0.200

Table 8: Intra and inter assay variability data (single wavelength) - Site 1: CCHMC Lot 2 611096.004.

Panel Members	Sample N	Grand Mean AL	Between-Day		Between-Tech		Total		Result
			SD	%CV	SD	%CV	SD	%CV	
PC	10	1.845	0.120	6.5%	0.109	5.9%	0.168	9.1%	Positive
NC	10	0.064	0.007	11.5%	0.005	8.3%	0.009	13.8%	Negative
MP 1	10	1.871	0.279	14.9%	0.052	2.8%	0.305	16.3%	Positive
MP 2	10	1.947	0.174	8.9%	0.217	11.2%	0.284	14.6%	Positive
MP 3	10	1.896	0.109	5.7%	0.237	12.5%	0.290	15.3%	Positive
LP 1	10	0.673	0.060	8.9%	0.126	18.7%	0.133	19.8%	Positive
LP 2	10	0.576	0.040	7.0%	0.051	8.9%	0.108	18.8%	Positive
LP 3	10	0.649	0.170	26.2%	0.048	7.4%	0.176	27.1%	Positive
HN 1	10	0.074	0.004	5.3%	0.008	10.7%	0.010	13.0%	Negative
HN 2	10	0.074	0.007	9.9%	0.011	14.3%	0.012	16.2%	Negative
HN 3	10	0.075	0.021	27.5%	0.018	24.5%	0.030	40.4%	Negative
WN 1	10	0.066	0.006	9.3%	0.001	2.1%	0.007	10.6%	Negative

Table 9: Intra and inter assay variability data (single wavelength) - Site 2: SHH Lot 1 611096.003.

Panel Members	Sample N	Grand Mean AL	Between-Day		Between-Tech		Total		Result
			SD	%CV	SD	%CV	SD	%CV	
PC	10	1.805	0.144	8.0%	0.053	3.0%	0.167	9.3%	Positive
NC	10	0.054	0.018	34.3%	0.022	41.0%	0.029	54.5%	Negative
MP 1	10	1.821	0.262	14.4%	0.187	10.2%	0.344	18.9%	Positive
MP 2	10	1.646	0.325	19.7%	0.002	0.1%	0.376	22.8%	Positive
MP 3	10	1.198	0.156	13.0%	0.045	3.8%	0.260	21.7%	Positive
LP 1	10	0.633	0.107	16.9%	0.054	8.5%	0.127	20.0%	Positive
LP 2	10	0.592	0.131	22.1%	0.006	1.0%	0.139	23.5%	Positive
LP 3	10	0.603	0.133	22.1%	0.052	8.6%	0.134	22.2%	Positive
HN 1	10	0.043	0.009	20.2%	0.005	10.4%	0.013	30.1%	Negative
HN 2	10	0.043	0.006	13.7%	0.006	13.5%	0.009	21.4%	Negative
HN 3	10	0.045	0.013	28.7%	0.010	22.4%	0.019	42.0%	Negative
WN 1	10	0.039	0.001	1.7%	0.001	2.5%	0.002	6.1%	Negative

Legend: PC=Positive control, NC=Negative control, MP=Moderate positive, LP=Low positive, HN=High negative, WN=Weak negative

Interpretation of Results at OD_{450}:

Positive Control: ≥ 0.600

Negative Control: < 0.150

Positive: ≥ 0.200

Negative: <0.200

Table 10: Intra and inter assay variability data (single wavelength) - Site 3: NCH Lot 3 611096.005.

Panel Members	Sample N	Grand Mean AL	Between-Day		Between-Tech		Total		Result
			SD	%CV	SD	%CV	SD	%CV	
PC	10	2.181	0.222	10.2%	0.127	5.8%	0.315	14.4%	Positive
NC	10	0.042	0.002	4.7%	0.002	4.4%	0.003	7.2%	Negative
MP 1	10	2.178	0.220	10.1%	0.278	12.8%	0.346	15.9%	Positive
MP 2	10	2.215	0.233	10.5%	0.226	10.2%	0.330	14.9%	Positive
MP 3	10	2.179	0.212	9.7%	0.224	10.3%	0.401	18.4%	Positive
LP 1	10	0.809	0.109	13.5%	0.107	13.3%	0.151	18.7%	Positive
LP 2	10	0.844	0.096	11.4%	0.143	16.9%	0.166	19.7%	Positive
LP 3	10	0.830	0.083	10.1%	0.139	16.8%	0.185	22.2%	Positive
HN 1	10	0.053	0.006	12.0%	0.007	14.1%	0.010	19.4%	Negative
HN 2	10	0.056	0.012	21.1%	0.005	8.5%	0.013	22.9%	Negative
HN 3	10	0.058	0.006	9.9%	0.002	3.9%	0.007	12.4%	Negative
WN 1	10	0.045	0.002	4.1%	0.001	3.2%	0.004	9.0%	Negative

Table 11: Reproducibility data (single wavelength) - Site 1: CCHMC, Lot 611096.004.

Sample ID	Sample Qual. Result	Day 1 Run 1 (DH)*	Day 1 Run 2 (MJG)*	Day 2 Run 1 (DH)*	Day 2 Run 2 (MJG)*	Day 3 Run 1 (DH)*	Day 3 Run 2 (MJG)*	Day 4 Run 1 (DH)*	Day 4 Run 2 (MJG)*	Day 5 Run 1 (DH)*	Day 5 Run 2 (MJG)*	Result
PC	N/A	1.756	2.038	1.868	1.725	1.495	1.820	1.820	2.081	1.898	1.946	Positive
NC		0.069	0.083	0.059	0.053	0.060	0.072	0.059	0.067	0.056	0.066	Negative
MP 1	1.930	1.694	1.549	2.099	2.072	1.307	1.728	2.241	1.967	1.829	2.223	Positive
MP 2		1.491	1.943	2.147	2.203	1.731	2.326	2.052	1.869	1.545	2.161	Positive
MP 3		1.598	2.111	2.092	1.698	1.482	2.093	1.944	2.209	1.524	2.204	Positive
LP 1	0.484	0.568	0.887	0.781	0.684	0.459	0.731	0.542	0.723	0.572	0.785	Positive
LP 2		0.452	0.669	0.726	0.500	0.484	0.548	0.601	0.623	0.434	0.719	Positive
LP 3		0.477	0.749	0.578	0.500	0.511	0.606	0.556	0.618	0.956	0.943	Positive
HN 1	0.003	0.063	0.085	0.070	0.089	0.066	0.086	0.075	0.063	0.069	0.076	Negative
HN 2		0.074	0.083	0.065	0.100	0.061	0.065	0.069	0.078	0.064	0.082	Negative
HN 3		0.059	0.061	0.057	0.069	0.067	0.064	0.062	0.086	0.063	0.157	Negative
WN 1	0.002	0.078	0.075	0.059	0.066	0.060	0.064	0.071	0.062	0.057	0.068	Negative
Average high negative value		0.065	0.076	0.064	0.086	0.065	0.072	0.069	0.076	0.065	0.105	
Average low positive value		0.499	0.768	0.695	0.561	0.485	0.628	0.566	0.655	0.654	0.816	
Percent Correlation		100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	
Correlation of cut off Specimens		100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	

Legend: PC=Positive control, NC=Negative control, MP=Moderate positive, LP=Low positive, HN=High negative, WN=Weak negative

* Initials of person performing testing.

Interpretation of Results at OD_{450}:

Positive Control: ≥ 0.600

Negative Control: < 0.150

Positive: ≥ 0.200

Negative: <0.200

Table 12: Reproducibility data (single wavelength) - Site 2: SHH, Lot 611096.003.

Sample ID	Sample Qual. Result	Day 1 Run 1 (DM)*	Day 1 Run 2 (JM)*	Day 2 Run 1 (DM)*	Day 2 Run 2 (JM)*	Day 3 Run 1 (DM)*	Day 3 Run 2 (JM)*	Day 4 Run 1 (DM)*	Day 4 Run 2 (JM)*	Day 5 Run 1 (DM)*	Day 5 Run 2 (JM)*	Result
PC	N/A	1.883	2.057	2.023	1.795	1.500	1.736	1.724	1.915	1.706	1.710	Positive
NC		0.037	0.038	0.038	0.039	0.037	0.077	0.040	0.066	0.039	0.127	Negative
MP 1	1.930	1.925	1.535	2.008	2.106	1.457	1.986	1.852	2.379	1.205	1.761	Positive
MP 2		1.679	1.466	2.400	1.741	1.015	1.506	1.856	1.889	1.275	1.636	Positive
MP 3		1.101	1.363	1.812	1.104	1.078	1.097	0.909	1.316	1.251	0.953	Positive
LP 1	0.484	0.724	0.578	0.657	0.894	0.432	0.534	0.621	0.710	0.543	0.640	Positive
LP 2		0.571	0.360	0.819	0.778	0.465	0.578	0.581	0.689	0.503	0.576	Positive
LP 3		0.461	0.512	0.795	0.864	0.530	0.553	0.519	0.685	0.526	0.585	Positive
HN 1	0.003	0.043	0.033	0.039	0.079	0.044	0.036	0.039	0.040	0.036	0.045	Negative
HN 2		0.043	0.040	0.038	0.067	0.037	0.037	0.039	0.048	0.037	0.043	Negative
HN 3		0.043	0.039	0.038	0.099	0.037	0.039	0.038	0.045	0.035	0.041	Negative
WN 1	0.002	0.037	0.042	0.043	0.037	0.036	0.041	0.037	0.040	0.039	0.039	Negative
Average high negative value		0.043	0.037	0.038	0.082	0.039	0.037	0.039	0.044	0.036	0.043	
Average low positive value		0.585	0.483	0.757	0.845	0.476	0.555	0.574	0.695	0.524	0.600	
Percent Correlation		100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	
Correlation of cut off Specimens		100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	

Legend: PC=Positive control, NC=Negative control, MP=Moderate positive, LP=Low positive, HN=High negative, WN=Weak negative

* Initials of person performing testing.

Interpretation of Results at OD_{450}:

Positive Control: ≥ 0.600

Negative Control: < 0.150

Positive: ≥ 0.200

Negative: <0.200

Table 13: Reproducibility data (single wavelength) - Site 3: NCH, Lot 611096.005.

Sample ID	Sample Qual. Result	Day 1 Run 1 (LS)*	Day 1 Run 2 (KE)*	Day 2 Run 1 (LS)*	Day 2 Run 2 (KE)*	Day 3 Run 1 (LS)*	Day 3 Run 2 (KE)*	Day 4 Run 1 (LS)*	Day 4 Run 2 (KE)*	Day 5 Run 1 (LS)*	Day 5 Run 2 (KE)*	Result
PC	N/A	1.962	2.365	2.126	2.551	2.665	2.110	2.174	2.213	1.528	2.117	Positive
NC		0.040	0.042	0.048	0.040	0.047	0.041	0.040	0.040	0.041	0.040	Negative
MP 1	1.930	1.995	2.376	2.133	2.822	2.199	2.125	2.157	2.261	1.425	2.290	Positive
MP 2		1.755	2.568	2.269	2.592	2.466	2.260	2.202	2.36	1.585	2.094	Positive
MP 3		1.667	2.845	1.892	2.372	2.589	2.038	2.373	2.347	1.582	2.083	Positive
LP 1	0.484	0.574	0.902	0.792	1.047	0.904	0.866	0.846	0.847	0.549	0.763	Positive
LP 2		0.587	1.037	0.741	0.976	0.976	0.909	0.849	0.969	0.560	0.832	Positive
LP 3		0.547	0.995	0.806	1.008	1.038	0.774	0.738	0.960	0.531	0.907	Positive
HN 1	0.003	0.041	0.058	0.070	0.059	0.045	0.056	0.045	0.057	0.038	0.062	Negative
HN 2		0.066	0.061	0.059	0.084	0.044	0.046	0.056	0.060	0.040	0.048	Negative
HN 3		0.056	0.061	0.074	0.056	0.051	0.047	0.061	0.057	0.056	0.061	Negative
WN 1	0.002	0.042	0.041	0.053	0.038	0.045	0.047	0.044	0.047	0.045	0.046	Negative
Average high negative value		0.054	0.060	0.068	0.066	0.047	0.050	0.054	0.058	0.045	0.057	
Average low positive value		0.569	0.978	0.780	1.010	0.973	0.850	0.811	0.925	0.547	0.834	
Percent Correlation		100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	
Correlation of cut off Specimens		100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	

Legend: PC=Positive control, NC=Negative control, MP=Moderate positive, LP=Low positive, HN=High negative, WN=Weak negative

* Initials of person performing testing.

Interpretation of Results at OD_{450}:

Positive Control: ≥ 0.600

Negative Control: < 0.150

Positive: ≥ 0.200

Negative: <0.200

Table 14: Intra and inter assay variability data for all sites (dual wavelength).

Panel Members	Sample N	Grand Mean AL	Between-Day		Between-Run		Between-Site		Total		Result
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	
PC	30	1.888	0.088	4.7%	0.121	6.4%	0.208	11.0%	0.276	14.6%	Positive
NC	30	0.012	0.007	55.3%	0.010	86.7%	0.008	64.0%	0.017	147.6%	Negative
MP 1	30	1.899	0.200	10.5%	0.253	13.3%	0.196	10.3%	0.356	18.7%	Positive
MP 2	30	1.881	0.197	10.5%	0.279	15.2%	0.281	14.9%	0.393	20.9%	Positive
MP 3	30	1.666	0.179	10.7%	0.239	14.3%	0.451	27.1%	0.540	32.4%	Positive
LP 1	30	0.659	0.066	10.1%	0.097	14.8%	0.093	14.2%	0.155	23.6%	Positive
LP 2	30	0.626	0.066	10.5%	0.090	14.4%	0.150	23.9%	0.183	29.3%	Positive
LP 3	30	0.647	0.053	8.2%	0.092	14.3%	0.116	17.9%	0.186	28.8%	Positive
HN 1	30	0.013	0.005	35.9%	0.005	38.3%	0.006	48.2%	0.011	81.7%	Negative
HN 2	30	0.016	0.008	54.0%	0.011	69.8%	0.009	56.4%	0.014	87.3%	Negative
HN 3	30	0.019	0.009	48.2%	0.013	69.9%	0.012	62.8%	0.025	131.6%	Negative
WN 1	30	0.008	0.001	9.8%	0.002	21.0%	0.006	81.2%	0.006	76.3%	Negative

Table 15: Intra and inter assay variability data (dual wavelength) - Site 1: CCHMC Lot 2 611096.004.

Panel Members	Sample N	Grand Mean AL	Between-Day		Between-Tech		Total		Result
			SD	%CV	SD	%CV	SD	%CV	
PC	10	1.780	0.116	6.5%	0.094	5.3%	0.163	9.1%	Positive
NC	10	0.013	0.003	19.5%	0.001	6.3%	0.003	20.9%	Negative
MP 1	10	1.801	0.273	15.1%	0.029	1.6%	0.294	16.3%	Positive
MP 2	10	1.885	0.172	9.1%	0.202	10.7%	0.278	14.7%	Positive
MP 3	10	1.841	0.108	5.9%	0.240	13.0%	0.298	16.2%	Positive
LP 1	10	0.619	0.056	9.1%	0.125	20.2%	0.132	21.3%	Positive
LP 2	10	0.528	0.043	8.2%	0.052	9.9%	0.109	20.6%	Positive
LP 3	10	0.599	0.170	28.4%	0.043	7.2%	0.177	29.5%	Positive
HN 1	10	0.020	0.006	29.1%	0.001	6.3%	0.008	41.6%	Negative
HN 2	10	0.025	0.010	41.2%	0.004	14.1%	0.013	50.6%	Negative
HN 3	10	0.033	0.027	81.0%	0.017	52.9%	0.036	109.3%	Negative
WN 1	10	0.015	0.002	13.7%	0.002	11.3%	0.004	29.3%	Negative

Legend: PC=Positive control, NC=Negative control, MP=Moderate positive, LP=Low positive, HN=High negative, WN=Weak negative

Interpretation of Results at OD $_{450/630}$:

Positive Control: ≥ 0.600

Negative Control: < 0.100

Positive: ≥ 0.150

Negative: < 0.150

Table 16: Intra and inter assay variability data (dual wavelength) - Site 2: SHH Lot 1 611096.003.

Panel Members	Sample N	Grand Mean AL	Between-Day		Between-Tech		Total		Result
			SD	%CV	SD	%CV	SD	%CV	
PC	10	1.757	0.141	8.0%	0.059	3.3%	0.165	9.4%	Positive
NC	10	0.019	0.018	97.6%	0.022	120.0%	0.029	157.3%	Negative
MP 1	10	1.772	0.260	14.7%	0.183	10.3%	0.341	19.2%	Positive
MP 2	10	1.599	0.322	20.1%	0.003	0.2%	0.370	23.1%	Positive
MP 3	10	1.154	0.154	13.4%	0.046	4.0%	0.256	22.2%	Positive
LP 1	10	0.592	0.106	17.9%	0.050	8.5%	0.125	21.1%	Positive
LP 2	10	0.553	0.129	23.4%	0.004	0.7%	0.137	24.9%	Positive
LP 3	10	0.564	0.133	23.5%	0.050	8.9%	0.133	23.5%	Positive
HN 1	10	0.008	0.009	106.4%	0.005	59.6%	0.013	152.1%	Negative
HN 2	10	0.008	0.006	82.6%	0.004	55.8%	0.009	120.3%	Negative
HN 3	10	0.011	0.013	125.0%	0.009	83.3%	0.019	179.1%	Negative
WN 1	10	0.003	0.001	24.2%	0.001	25.0%	0.001	42.1%	Negative

Table 17: Intra and inter assay variability data (dual wavelength) - Site 3: NCH Lot 3 611096.005.

Panel Members	Sample N	Grand Mean AL	Between-Day		Between-Tech		Total		Result
			SD	%CV	SD	%CV	SD	%CV	
PC	10	2.128	0.218	10.2%	0.132	6.2%	0.310	14.6%	Positive
NC	10	0.004	0.001	22.8%	0.000	7.9%	0.001	26.8%	Negative
MP 1	10	2.126	0.219	10.3%	0.277	13.0%	0.345	16.2%	Positive
MP 2	10	2.160	0.231	10.7%	0.227	10.5%	0.327	15.2%	Positive
MP 3	10	2.003	0.475	23.7%	0.049	2.4%	0.578	28.9%	Positive
LP 1	10	0.766	0.119	15.5%	0.119	15.5%	0.159	20.8%	Positive
LP 2	10	0.798	0.094	11.7%	0.147	18.4%	0.166	20.8%	Positive
LP 3	10	0.779	0.095	12.1%	0.133	17.1%	0.182	23.4%	Positive
HN 1	10	0.011	0.006	55.8%	0.004	36.7%	0.007	66.2%	Negative
HN 2	10	0.014	0.011	73.8%	0.009	64.3%	0.014	94.8%	Negative
HN 3	10	0.014	0.007	47.6%	0.002	14.3%	0.008	57.4%	Negative
WN 1	10	0.005	0.001	20.9%	0.001	20.2%	0.002	37.8%	Negative

Legend: PC=Positive control, NC=Negative control, MP=Moderate positive, LP=Low positive, HN=High negative, WN=Weak negative

Interpretation of Results at OD $_{450/630}$:

Positive Control: ≥ 0.600

Negative Control: < 0.100

Positive: ≥ 0.150

Negative: < 0.150

Table 18: Reproducibility data (dual wavelength) - Site 1: CCHMC, Lot 611096.004.

Sample ID	Sample Qual. Result	Day 1 Run 1 (DH)*	Day 1 Run 2 (MJG)*	Day 2 Run 1 (DH)*	Day 2 Run 2 (MJG)*	Day 3 Run 1 (DH)*	Day 3 Run 2 (MJG)*	Day 4 Run 1 (DH)*	Day 4 Run 2 (MJG)*	Day 5 Run 1 (DH)*	Day 5 Run 2 (MJG)*	Result
PC	N/A	1.684	1.968	1.827	1.663	1.432	1.757	1.770	1.992	1.857	1.854	Positive
NC		0.011	0.009	0.012	0.013	0.012	0.013	0.016	0.017	0.013	0.018	Negative
MP 1	1.930	1.642	1.469	2.052	1.985	1.258	1.660	2.170	1.896	1.781	2.097	Positive
MP 2		1.427	1.886	2.096	2.120	1.676	2.261	2.008	1.801	1.505	2.071	Positive
MP 3		1.524	2.039	2.045	1.631	1.419	2.031	1.888	2.137	1.481	2.213	Positive
LP 1	0.484	0.510	0.840	0.716	0.622	0.412	0.681	0.483	0.670	0.529	0.722	Positive
LP 2		0.398	0.626	0.678	0.445	0.439	0.493	0.547	0.602	0.390	0.657	Positive
LP 3		0.423	0.704	0.530	0.434	0.469	0.555	0.509	0.565	0.910	0.886	Positive
HN 1	0.003	0.015	0.008	0.028	0.012	0.012	0.032	0.021	0.019	0.030	0.026	Negative
HN 2		0.024	0.007	0.027	0.053	0.014	0.016	0.020	0.035	0.028	0.027	Negative
HN 3		0.019	0.015	0.018	0.021	0.015	0.017	0.026	0.040	0.025	0.133	Negative
WN 1	0.002	0.020	0.010	0.012	0.019	0.006	0.017	0.016	0.017	0.015	0.018	Negative
Average high negative value		0.019	0.010	0.024	0.029	0.014	0.022	0.022	0.031	0.028	0.062	
Average low positive value		0.444	0.723	0.641	0.500	0.440	0.576	0.513	0.612	0.610	0.755	
Percent Correlation		100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	
Correlation of cut off Specimens		100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	

Legend: PC=Positive control, NC=Negative control, MP=Moderate positive, LP=Low positive, HN=High negative, WN=Weak negative

* Initials of person performing testing.

Interpretation of Results at OD $_{450/630}$:

Positive Control: ≥ 0.600

Negative Control: < 0.100

Positive: ≥ 0.150

Negative: < 0.150

Table 19: Reproducibility data (dual wavelength) - Site 2: SHH, Lot 611096.003.

Sample ID	Sample Qual. Result	Day 1 Run 1 (DM)*	Day 1 Run 2 (JM)*	Day 2 Run 1 (DM)*	Day 2 Run 2 (JM)*	Day 3 Run 1 (DM)*	Day 3 Run 2 (JM)*	Day 4 Run 1 (DM)*	Day 4 Run 2 (JM)*	Day 5 Run 1 (DM)*	Day 5 Run 2 (JM)*	Result
PC	N/A	1.834	1.998	1.965	1.773	1.448	1.709	1.666	1.864	1.664	1.648	Positive
NC		0.002	0.004	0.003	0.004	0.003	0.043	0.003	0.029	0.003	0.091	Negative
MP 1	1.930	1.882	1.487	1.955	2.060	1.412	1.940	1.804	2.314	1.157	1.705	Positive
MP 2		1.630	1.419	2.333	1.697	0.978	1.457	1.815	1.846	1.229	1.585	Positive
MP 3		1.060	1.314	1.758	1.063	1.038	1.049	0.870	1.273	1.205	0.909	Positive
LP 1	0.484	0.685	0.539	0.617	0.850	0.395	0.494	0.582	0.664	0.504	0.591	Positive
LP 2		0.533	0.323	0.779	0.736	0.429	0.538	0.544	0.644	0.465	0.535	Positive
LP 3		0.424	0.474	0.755	0.825	0.493	0.513	0.483	0.638	0.485	0.546	Positive
HN 1	0.003	0.008	0.004	0.004	0.044	0.005	0.003	0.004	0.004	0.003	0.004	Negative
HN 2		0.009	0.005	0.004	0.033	0.003	0.003	0.005	0.006	0.002	0.006	Negative
HN 3		0.009	0.005	0.004	0.065	0.003	0.005	0.004	0.005	0.002	0.005	Negative
WN 1	0.002	0.003	0.002	0.004	0.004	0.003	0.003	0.003	0.003	0.007	0.002	Negative
Average high negative value		0.009	0.005	0.004	0.047	0.004	0.004	0.004	0.005	0.002	0.005	
Average low positive value		0.547	0.445	0.717	0.804	0.439	0.515	0.536	0.649	0.485	0.557	
Percent Correlation		100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	
Correlation of cut off Specimens		100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	

Legend: PC=Positive control, NC=Negative control, MP=Moderate positive, LP=Low positive, HN=High negative, WN=Weak negative

* Initials of person performing testing.

Interpretation of Results at OD $_{450/630}$:

Positive Control: ≥ 0.600

Negative Control: < 0.100

Positive: ≥ 0.150

Negative: < 0.150

Table 20: Reproducibility data (dual wavelength) - Site 3: NCH, Lot 611096.005.

Sample ID	Sample Qual. Result	Day 1 Run 1 (LS)*	Day 1 Run 2 (KE)*	Day 2 Run 1 (LS)*	Day 2 Run 2 (KE)*	Day 3 Run 1 (LS)*	Day 3 Run 2 (KE)*	Day 4 Run 1 (LS)*	Day 4 Run 2 (KE)*	Day 5 Run 1 (LS)*	Day 5 Run 2 (KE)*	Result
PC	N/A	1.911	2.311	2.075	2.496	2.587	2.063	2.123	2.163	1.476	2.071	Positive
NC		0.003	0.004	0.004	0.003	0.006	0.004	0.003	0.003	0.003	0.003	Negative
MP 1	1.930	1.951	2.322	2.080	2.762	2.146	2.076	2.099	2.21	1.371	2.238	Positive
MP 2		1.711	2.514	2.205	2.538	2.411	2.212	2.136	2.304	1.535	2.038	Positive
MP 3		1.621	2.784	1.842	2.321	2.531	1.990	2.317	2.292	1.532	0.802	Positive
LP 1	0.484	0.533	0.855	0.747	1.005	0.858	0.823	0.794	0.855	0.476	0.710	Positive
LP 2		0.539	0.995	0.702	0.934	0.932	0.869	0.780	0.922	0.521	0.790	Positive
LP 3		0.497	0.950	0.770	0.963	0.983	0.734	0.689	0.917	0.487	0.802	Positive
HN 1	0.003	0.008	0.018	0.022	0.018	0.004	0.005	0.004	0.015	0.002	0.012	Negative
HN 2		0.010	0.021	0.014	0.049	0.005	0.006	0.007	0.019	0.003	0.009	Negative
HN 3		0.006	0.022	0.030	0.019	0.008	0.006	0.010	0.016	0.008	0.013	Negative
WN 1	0.002	0.005	0.003	0.009	0.003	0.005	0.007	0.004	0.004	0.005	0.004	Negative
Average high negative value		0.008	0.020	0.022	0.029	0.006	0.006	0.007	0.017	0.004	0.011	
Average low positive value		0.523	0.933	0.740	0.967	0.924	0.809	0.754	0.898	0.495	0.767	
Percent Correlation		100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	
Correlation of cut off Specimens		100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	

Legend: PC=Positive control, NC=Negative control, MP=Moderate positive, LP=Low positive, HN=High negative, WN=Weak negative

* Initials of person performing testing.

Interpretation of Results at OD $_{450/630}$:

Positive Control: ≥ 0.600

Negative Control: < 0.100

Positive: ≥ 0.150

Negative: < 0.150

Conclusions

The Premier *C. difficile* GDH assay can be used to screen human stool samples for *C. difficile* glutamate dehydrogenase and can be considered substantially equivalent to the reference method and predicate device.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

MAY - 3 2011

Meridian Bioscience, Inc.
c/o Ms. Susan Bogar
Product Quality Assurance Manager
3471 River Hills Drive
Cincinnati, OH 45244

Re: K110620
Trade/Device Name: Premier™ C. *difficile* GDH Assay
Regulation Number: 21 CFR 866.2660
Regulation Name: Microorganism differentiation and identification device.
Regulatory Class: Class I
Product Code: MCB
Dated: March 2, 2011
Received: March 3, 2011

Dear Ms. Bogar:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into class II (Special Controls), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

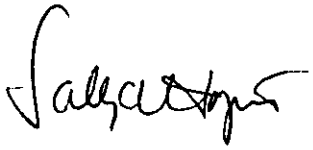
Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter

will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,



Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K110620

Device Name: Premier *C. difficile* GDH

Indications for Use:

Premier *C. difficile* GDH is a qualitative enzyme immunoassay screening test to detect *Clostridium difficile* antigen, glutamate dehydrogenase, in fecal specimens from symptomatic persons suspected of having *C. difficile* infection (CDI). This test does not distinguish between toxigenic and non-toxigenic strains of *C. difficile*. Samples from symptomatic patients that produce positive results with this test must be further tested with an assay designed to detect toxigenic *C. difficile* strains and assist with the diagnosis of CDI.

Prescription Use ___X____ (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE OF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K110620